

Amendments to The Claims

The following listing of claims replaces all prior versions and listings of the claims in this application.

Listing of the Claims

1-193. (Cancelled)

194. (Previously presented) A method for identifying a compound that potentially modulates T1R1/T1R3 (umami) receptor-associated taste in a subject comprising:

(i) screening one or more compounds in a functional assay that detects compounds which modulate (enhance or inhibit) the activity of the T1R1/T1R3 receptor by another compound; and

(ii) identifying compounds that potentially modulate T1R1/T1R3 (umami) receptor-associated taste based on their modulation (enhancement or inhibition) of the activity of the T1R1/T1R3 (umami) taste receptor by another compound, wherein said T1R1 is a T1R1 polypeptide and is (i) encoded by a nucleic acid sequence comprising SEQ. ID. NO: 8, (ii) encoded by a nucleic acid sequence comprising a nucleic acid that hybridizes to SEQ. ID. NO: 8 under stringent hybridization conditions which are conducting the hybridization reaction at 42°C in a solution comprising 50% formamide, 5X SSC, and 1% SDS and washing at 65°C in a solution comprising 0.2X SSC and 0.1% SDS, or (iii) a T1R1 polypeptide possessing at least 95% sequence identity to the T1R1 polypeptide of SEQ. ID. NO: 5;

and wherein said T1R3 is a T1R3 polypeptide and is (i) encoded by a nucleic acid sequence comprising SEQ. ID. NO: 9 or SEQ. ID. NO: 11; (ii) encoded by a nucleic acid sequence that hybridizes to SEQ. ID. NO: 9 or SEQ. ID. NO: 11 under stringent hybridization conditions which are conducting the hybridization reaction at 42°C in a solution comprising 50% formamide, 5X SSC, 10% SDS; and washing at 65°C in a solution comprising 0.2X SCC and 0.1% SDS, or (iii) a T1R3 polypeptide possessing at least 95% sequence identity to the T1R3 polypeptide of SEQ. ID. NO: 4 or SEQ. ID. NO: 7.

195. (Previously presented) The method of claim 194 wherein said T1R1 receptor is selected from the group consisting of rat T1R1, mouse T1R1 and human T1R1 and said T1R3 receptor is selected from the group consisting of rat T1R3, mouse T1R3 and human T1R3.

196. (Previously presented) The method of claim 194 wherein said T1R1 and T1R3 are of the same species origin.

197. (Previously presented) The method of claim 194 wherein said T1R1 and T1R3 are of different species origin.

198. (Previously presented) The method of claim 194 wherein said T1R1 is a human T1R1 polypeptide comprising the amino acid sequence of SEQ. ID. NO: 5.

199. (Canceled)

200. (Previously presented) The method of claim 194 wherein said T1R1 is a human T1R1 polypeptide that exhibits at least 95% sequence identity to the polypeptide of SEQ. ID NO: 5.

201. (Previously presented) The method of claim 194 wherein said T1R1 is a human T1R1 polypeptide that exhibits at least 96% sequence identity to the polypeptide of SEQ. ID NO: 5.

202. (Previously presented) The method of claim 194 wherein said T1R1 is a human T1R1 polypeptide that exhibits at least 97% sequence identity to the polypeptide of SEQ. ID NO: 5.

203. (Previously presented) The method of claim 194 wherein said T1R1 is a human T1R1 polypeptide that exhibits at least 98% sequence identity to the polypeptide of SEQ. ID NO: 5.

204. (Previously presented) The method of claim 194 wherein said T1R1 is a human T1R1 polypeptide that exhibits at least 99% sequence identity to the polypeptide of SEQ. ID NO: 5.

205. (Previously presented) The method of claim 194 wherein said T1R1 is encoded by the nucleic acid sequence of SEQ. ID. NO: 8.

206. (Previously presented) The method of claim 194 which said T1R1 is encoded by a nucleic acid sequence that hybridizes to SEQ. ID. NO: 8 under stringent hybridization conditions which are conducting the hybridization reaction at 42°C in a solution comprising 50% formamide, 5X SSC, and 1% SDS and washing at 65°C in a solution comprising 0.2X SSC and 0.1% SDS.

207. (Canceled)

208. (Canceled)

209. (Previously presented) The method of claim 194 wherein said T1R3 is a human T1R3 polypeptide comprising the amino acid sequence of SEQ. ID. NO: 7.

210. (Canceled)

211. (Previously presented) The method of claim 194, wherein said T1R3 is a human T1R3 polypeptide that possesses at least 95% sequence identity to the polypeptide of SEQ. ID. NO: 7.

212. (Previously presented) The method of claim 194, wherein said T1R3 is a human T1R3 polypeptide that possesses at least 96% sequence identity to the polypeptide of SEQ. ID. NO: 7.

213. (Previously presented) The method of claim 194, wherein said T1R3 is a human T1R3 polypeptide that possesses at least 97% sequence identity to the polypeptide of SEQ. ID. NO: 7.

214. (Previously presented) The method of claim 194, wherein said T1R3 is a human T1R3 polypeptide that possesses at least 98% sequence identity to the polypeptide of SEQ. ID. NO: 7.

215. (Previously presented) The method of claim 194, wherein said T1R3 is a human T1R3 polypeptide that possesses at least 99% sequence identity to the polypeptide of SEQ. ID. NO: 7.

216. (Previously presented) The method of claim 194 which said T1R3 is a rat T1R3 polypeptide comprising the sequence of SEQ. ID. NO: 4.

217. (Previously presented) The method of claim 194 which said T1R3 is encoded by the nucleic acid sequence of SEQ ID. NO: 9.

218. (Previously presented) The method of claim 194 wherein said T1R3 is encoded by a nucleic acid sequence that hybridizes to SEQ. ID. NO: 9 or SEQ. ID. NO: 11 under stringent hybridization conditions which are conducting the hybridization reaction at 42°C in a solution comprising 50% formamide, 5X SSC, and 1% SDS and washing at 65°C in a solution comprising 0.2X SSC and 0.1% SDS.

219. (Previously presented) The method of claim 194 wherein said T1R1 and T1R3 sequences are expressed in a cell.

220. (Previously presented) The method of claim 194 wherein said cell is intact or permeabilized.

221. (Previously presented) The method of claim 194 wherein a membrane extract comprises said T1R1/T1R3 receptor.

222. (Previously presented) The method of claim 219 wherein said T1R1 and T1R3 receptor sequences are expressed on the surface of said cell.

223. (Previously presented) The method of claim 219 wherein the cell is a eukaryotic cell.

224. (Previously presented) The method of claim 219 wherein the cell is a prokaryotic cell.

225. (Previously presented) The method of claim 223 wherein the eukaryotic cell is a yeast, insect, amphibian or mammalian cell.

226. (Previously presented) The method of claim 223 wherein the cell is a CHO cell, COS cell, HEK-293 cell or Xenopus oocyte.

227. (Previously presented) The method of claim 219 wherein the cell further expresses a G protein.

228. (Previously presented) The method of claim 227 wherein said G protein is $G_{\alpha 15}$, $G_{\alpha 16}$ or gustducin.

229. (Previously presented) The method of claim 194 wherein said functional assay detects the effect of said compound on phosphorylation of said T1R1/T1R3 receptors.

230. (Previously presented) The method of claim 194 wherein said functional assay detects the effect of said compound on the internalization of said T1R1/T1R3 receptors.

231. (Previously presented) The method of claim 194 wherein said functional assay detects the effect of said compound on arrestin translocation.

232. (Currently amended) The method of claim 194 wherein said functional assay detects the effect of ~~on~~ said compound on second messengers.

233. (Previously presented) The method of claim 232 wherein said second messenger is cAMP, cGMP or IP3.

234. (Previously presented) The method of claim 194 wherein said functional assay detects changes in voltage or intracellular calcium.

235. (Previously presented) The method of claim 234 wherein said functional assay includes the use of a voltage-sensitive or calcium-sensitive dye.

236. (Previously presented) The method of claim 194 wherein the functional assay detects the effect of said compound on G protein activation by said T1R1/T1R3 receptor.

237. (Previously presented) The method of claim 194 wherein said T1R1 and T1R3 sequences are linked to a reporter gene.

238. (Previously presented) The method of claim 237 wherein said reporter gene luciferase, alkaline phosphatase, or Beta-galactosidase.

239. (Previously presented) The method of claim 194 wherein a synthetic compound library comprises said one or more compounds.

240. (Previously presented) The method of claim 194 wherein a combinatorial compound library comprises said one or more compounds.

241. (Previously presented) The method of claim 194 wherein said one or more compounds are compounded in a randomized library of small molecules.

242. (Currently amended) The method of claim 194 wherein the step of screening is carried out by said method is a high-throughout the screening method.

243. (Previously presented) The method of claim 194 wherein the functional assay screens for compounds that enhance or inhibit the activity of the T1R1/T1R3 umami taste receptor by L- glutamate.

244. (Previously presented) The method of claim 194 wherein the functional assay screens for compounds that enhance or inhibit the binding of IMP, GMP or an analog thereof to the T1R1/T1R3 umami taste receptor.

245. (Previously presented) The method of claim 194 wherein the functional assay screens for compounds that modulate inhibition of the T1R1/T1R3 umami taste receptor activity by lactisole.

246. (Previously presented) The method of claim 194 wherein said functional assay detects the effect of said compound on signal transduction.

247. (Previously presented) The method of claim 194 wherein said functional assay detects changes in cellular polarization.

248. (Previously presented) The method of claim 247 wherein said changes are detected by voltage-clamp or patch-clamp technique.

249. (Currently amended) The method of claim 194 wherein the functional assay is a $\text{GTP}\gamma^{35}\text{S}$ assay.

250. (Previously presented) The method of claim 194 wherein said assay is a fluorescent polarization or FRET assay.

251. (Previously presented) The method of claim 194 wherein said assay detects changes in adenylate cyclase activity.

252. (Previously presented) The method of claim 194 wherein said functional assay detects the effect of said compound on ligand-specific coupling of said T1R1/T1R3 receptor with a G protein.

253. (Currently amended) The method of claim 194 wherein said functional assay detects the effects of said compound on a neurotransmitter or hormone release.

254. (Previously presented) The method of claim 194 wherein said T1R1/T1R3 taste receptor is stably expressed by a cell.

255. (Previously presented) The method of claim 194 wherein said T1R1/T1R3 taste receptor is transiently expressed by a cell.

256. (Previously presented) The method of which 194 wherein said T1R1 and T1R3 sequences are expressed under the control of an inducible promoter.

257. (Currently amended) A method for identifying a compound that potentially modulates T1R1/T1R3 (umami) receptor-associated taste in a subject comprising:

(i) screening one or more compounds in a functional assay that detects compounds which modulate (enhance or inhibit) the activity of the T1R1/T1R3 receptor by another compound; and

(ii) identifying compounds that potentially modulate T1R1/T1R3 (umami) receptor-associated taste based on their modulation (enhancement or inhibition) of the activity of the T1R1/T1R3 (umami) taste receptor by another compound, wherein said T1R1 is a T1R1 polypeptide possessing at least 95% sequence identity to native ~~the~~ human, mouse, or rat T1R1 polypeptide of Figure 1; and wherein said T1R3 is a T1R3 polypeptide possessing at least 95% sequence identity to native ~~the~~ human, mouse, or rat T1R3 polypeptide of Figure 1.

258. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R1 and T1R3 are derived from different species.

259. (Previously presented) The method of claim 257 wherein said T1R1 and T1R3 are of the same species.

260. (Currently amended) The method ~~cell~~ of claim 257 wherein T1R1 polypeptide is the human, ~~mouse~~, or rat T1R1 of Figure 1.

261. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R1 polypeptide has at least 95% sequence identity to the human, ~~mouse~~, or rat T1R1 of Figure 1.

262. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R1 polypeptide has at least 96% sequence identity to the human, ~~mouse~~, or rat T1R1 of Figure 1.

263. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R1 polypeptide has at least 97% sequence identity to the human, ~~mouse~~, or rat T1R1 of Figure 1.

264. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R1 polypeptide has at least 98% sequence identity to the human, ~~mouse~~, or rat T1R1 of Figure 1.

265. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R1 polypeptide has at least 99% sequence identity to the human, ~~mouse~~, or rat T1R1 of Figure 1.

266. (Currently amended) The method ~~cell~~ of claim 257 wherein T1R3 polypeptide is the human, ~~mouse~~, or rat T1R3 of Figure 1.

267. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R3 polypeptide has at least 95% sequence identity to the human,~~mouse~~, or rat T1R3 of Figure 1.

268. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R3 polypeptide has at least 96% sequence identity to the human,~~mouse~~, or rat T1R3 of Figure 1.

269. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R3 polypeptide has at least 97% sequence identity to the human,~~mouse~~, or rat T1R3 of Figure 1.

270. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R3 polypeptide has at least 98% sequence identity to the human,~~mouse~~, or rat T1R3 of Figure 1.

271. (Currently amended) The method ~~cell~~ of claim 257 wherein said T1R3 polypeptide has at least 99% sequence identity to the human,~~mouse~~, or rat T1R3 of Figure 1.

272. (Previously presented) The method of claim 257 wherein said T1R1 and T1R3 sequences are expressed in a cell.

273. (Currently amended) The method of claim 272 ~~257~~ wherein said cell is intact or permeabilized.

274. (Previously presented) The method of claim 257 wherein a membrane extract comprises said T1R1/T1R3 receptor.

275. (Previously presented) The method of claim 272 wherein said T1R1 and T1R3 receptor sequences are expressed on the surface of said cell.

276. (Previously presented) The method of claim 272 wherein the cell is a eukaryotic cell.

277. (Previously presented) The method of claim 272 wherein the cell is a prokaryotic cell.

278. (Previously presented) The method of claim 276 wherein the eukaryotic cell is a yeast, insect, amphibian or mammalian cell.

279. (Previously presented) The method of claim 276 wherein the cell is a CHO cell, COS cell, HEK-293 cell or Xenopus oocyte.

280. (Previously presented) The method of claim 272 wherein the cell further expresses a G protein.

281. (Previously presented) The method of claim 280 wherein said G protein is G_{a15} , G_{a16} or gustducin.

282. (Previously presented) The method of claim 257 wherein said functional assay detects the effect of said compound on phosphorylation of said T1R1/T1R3 receptors.

283. (Previously presented) The method of claim 257 wherein said functional assay detects the effect of said compound on the internalization of said T1R1/T1R3 receptors.

284. (Previously presented) The method of claim 257 wherein said functional assay detects the effect of said compound on arrestin translocation.

285. (Currently amended) The method of claim 257 wherein said functional assay detects the effect of ~~on~~ said compound on second messengers.

286. (Previously presented) The method of claim 285 wherein said second messenger is cAMP, cGMP or IP3.

287. (Previously presented) The method of claim 257 wherein said functional assay detects changes in voltage or intracellular calcium.

288. (Previously presented) The method of claim 287 wherein said functional assay includes the use of a voltage-sensitive or calcium-sensitive dye.

289. (Previously presented) The method of claim 257 wherein the functional assay detects the effect of said compound on G protein activation by said T1R1/T1R3 receptor.

290. (Previously presented) The method of claim 257 wherein said T1R1 and T1R3 sequences are linked to a reporter gene.

291. (Currently amended) The method of claim 290 wherein said reporter gene is luciferase, alkaline phosphatase, or Beta-galactosidase.

292. (Previously presented) The method of claim 257 wherein a synthetic compound library comprises said one or more compounds.

293. (Previously presented) The method of claim 257 wherein a combinatorial compound library comprises said one or more compounds.

294. (Previously presented) The method of claim 257 wherein said one or more compounds are compounded in a randomized library of small molecules.

295. (Currently amended) The method of claim 257 wherein the step of screening is carried out by is a high-throughput ~~the~~ screening method

296. (Previously presented) The method of claim 257 wherein the functional assay screens for compounds that enhance or inhibit the activity of the T1R1/T1R3 umami taste receptor by L- glutamate.

297. (Previously presented) The method of claim 257 wherein the functional assay screens for compounds that enhance or inhibit the binding of IMP, GMP or an analog thereof to the T1R1/T1R3 umami taste receptor.

298. (Previously presented) The method of claim 257 wherein the functional assay screens for compounds that modulate inhibition of the T1R1/T1R3 umami taste receptor activity by lactisole.

299. (Previously presented) The method of claim 257 wherein said functional assay detects the effect of said compound on signal transduction.

300. (Previously presented) The method of claim 257 wherein said functional assay detects changes in cellular polarization.

301. (Previously presented) The method of claim 300 wherein said changes are detected by voltage-clamp or patch-clamp technique.

302. (Previously presented) The method of claim 257 wherein the functional assay is a GTP γ ³⁵S assay.

303. (Previously presented) The method of claim 257 wherein said assay is a fluorescent polarization or FRET assay.

304. (Previously presented) The method of claim 257 wherein said assay detects changes in adenylate cyclase activity.

305. (Currently amended) The method of claim 257 wherein said functional assay detects the effect of said compound on ligand-specific coupling of said T1R1/T1R3 receptor with a G protein.

306. (Currently amended) The method of claim 257 wherein said functional assay detects the effects of said compound on a neurotransmitter or hormone release.

307. (Previously presented) The method of claim 257 wherein said T1R1/T1R3 taste receptor is stably expressed by a cell.

308. (Previously presented) The method of claim 257 wherein said T1R1/T1R3 taste receptor is transiently expressed by a cell.

309. (Previously presented) The method of which 257 wherein said T1R1 and T1R3 sequences are expressed under the control of an inducible promoter.